Global One Health Initiative: Projects

1. Characterization and optimization of hepatitis E virus replication in cell culture

The hepatitis E virus (HEV) infection is a zoonosis, which can be transmitted through contact with infected pigs and wild boars or consumption of food prepared thereof. Many aspects of HEV replication and stability are not known due to the lack of efficient cell culture systems for HEV so far. In the project, replication of a recently isolated HEV strain in cell culture will be investigated and optimized. Basic aspects of virus replication will be analyzed and a reverse genetics system will be established. Markers will be inserted into the HEV genome, which should allow the use of the virus in screening systems.

The project will integrate partners from human and animal medicine and should provide tools to study infectivity, inactivation and antiviral substances for a zoonotic virus with increasing importance.

2. Comparison of data on antimicrobial resistance from various surveillance and monitoring systems in veterinary and human medicine in Germany

Improvement of surveillance and monitoring systems is a key objective of the German antimicrobial resistance strategy (DART 2020) and the European action plan to combat antimicrobial resistance. Yet, currently the systems established in human medicine and veterinary medicine are separate entities and even within the fields several systems exist in parallel. Limited information is available on the comparability of the data on the national and regional level. Therefore the objective of the project is to address the following questions:

1. Are data from the different systems in veterinary and human medicine comparable?
2. Do the data allow for an estimate of the transfer of resistant bacteria and resistance determinants between the different populations?
3. How can we further improve comparability of the data to better suit the purpose of question no. 2
4. Is a common digital system for surveillance and monitoring possible to continuously analyse the data and generate early warnings in case of extraordinary developments in the data.

To address these questions available data from the two populations in Germany that are continuously collected by the groups of the two project leaders from BfR and RKI will be analysed thoroughly with respect to resistance profiles, as well as regional and temporal changes in resistance. The objective is to optimize the usability of the data and to potentially better assess the exchange of resistance determinants between populations using routinely collected data.

3. Luminex-based serological diagnosis of Toxoplasma gondii (T. gondii) infections and the differentiation of the acute and chronic infection stage

The PhD student will work on a collaborative research project between FLI, RKI and BfR. The research is aiming at improving T. gondii diagnostic tools. In close collaboration with the RKI, Luminex-based diagnostic tests will be developed for animals as well as humans using either recombinant T. gondii antigens or recombinant multi-epitope proteins. Furthermore these tests should be included as modules in multiplex-diagnostic tools, which will allow for simultaneously testing of various diseases. Finally a technique should be established able to differentiate the stages of Toxoplasma gondii infection (acute, chronic).

4. Understanding the zoonotic Hepatitis E virus (HEV-Rabbit) infections in animals: Establishment of a reverse genetic system of subgenomic HEV sequences and studies about the virulence for different mammals

HEV causes acute hepatitis E in humans in developing countries, but sporadic and autochthonous cases also occur in industrialized countries. Genotypes 3 and 4 have been found in humans as well as in animals (pigs, rabbits etc.) and are responsible for the increasing number of sporadic HEV cases in humans in industrialized countries and underscore the zoonotic potential of the virus. In general the infections in humans are asymptomatic, but fulminant hepatitis can occur in pregnant women and immunosuppressed patients. The PhD student will work on a collaborative research project between the FLI, BfR and RKI. In a first step, the sequence of recently described rabbit isolates will be determined and comprehensively phylogenetically analyzed. Based on the sequence information, a reverse genetic system is to be established and assessed for replication in a cell culture system. Furthermore, original and in vitro generated HEV isolates will be analyzed in infection studies in pigs and/or in rabbits.

5. Identification of cellular sensors and RNA signatures of ebolavirus (EBOV)

The PhD student will work on a collaborative research project between the König lab at the Paul-Ehrlich-Institut and the Hoenen lab at the Friedrich-Loeffler-Institut. The goal is to identify cellular immune sensors and regulators that detect EBOV. We hypothesize that these factors are crucial determinants for EBOV disease outcome and will be important determinants for future therapeutic interventions **and** vaccine design. The project will integrate research on EBOV and the study of innate immunity pathways using screening technologies (RNAi, CRISPR/Cas), proteomics as well more traditional cell & molecular biology and biochemistry approaches. It involves the use of virus-like particles amenable to study the ebolavirus replication cycle under BSL2 conditions.

6. Characterizing the role of antigenic diversity in mumps vaccine efficacy

The PhD student will work on a collaborative research project between the von Messling group at Paul-Ehrlich-Institut and the Mankertz group at Robert-Koch Institut. Over the last years, the incidence of mumps virus infections in young adults with complete immunization is on the rise. We hypothesize that antigenic divergence between currently circulating field isolates and vaccine strains contribute to this apparent lack of vaccine efficacy. To test this hypothesis, genotype and glycoprotein-specific antisera will be produced, and their cross-reactivity will first be analyzed in vitro. To gain insights in the protective efficacy of the induced immune response against different genotypes, an immunosuppressed mouse model for mumps virus will be established.

7. Genome-wide association studies in Klebsiella pneumoniae for the detection of possible host association, host adaptation and effects on virulence and antibiotic resistance

Among Gram-negative bacteria, the highest threat level comes along with carbapenemase-producing Klebsiella pneumoniae strains showing (i) an increased mortality i; (ii) limited treatment options and (iii) a high tendency of spread of distinct clones. The population structure of K. pneumoniae was investigated recently analysing isolates from various sources and from colonizations and infections. It became evident that “successful” strain types exist, being highly prevalent among the different habitats. Within this research project we aim at identifying aspects of niche adaptation and separation and try explaining the “epidemic success” of distinct strains. We combine functional genomics approaches with classical models investigating host-pathogen interactions (adhesion, invasion, etc.).

8. Development of reagents and serological tests for detection and tracking of sources of Toxoplasma gondii infections: a one-health approach

The high rate of toxoplasma seroprevalence in the German adult population is largely attributed to the consumption of raw meat or meat products from infected animals.
Reliable, scalable (and affordable) methods are needed to assess both the levels of oocysts infected humans and animals as well as the number of oocysts in the environment. Therefore, the methodology for the enrichment of oocysts from environmental samples via immunoaffinity chromatography needs to be optimized. It is planned to generate recombinant antibody fragments (so-called camelid single-domain proteins, or nanobodies) against oocysts, which are more robust compared to conventional antibodies in order to bind to oocysts under the assay conditions.
A second approach is to validate four known oocyst-specific proteins for their suitability as serological markers for acute infection with oocysts.